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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/585,772	11/13/2007	Aiping H. Young	50120/008001	4680

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EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

NOTIFICATION DATE	DELIVERY MODE
08/30/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/585,772	YOUNG ET AL.	
	Examiner	Art Unit	
	DANA SHIN	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,23-26,32,33 and 52-71* is/are pending in the application.

4a) Of the above claim(s) *1-17 and 52-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,23-26,32,33 and 56-71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5-25-2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 5, 2010 has been entered.

Status of Claims

Claims 1-18, 23-26, 32-33, and 52-71 are pending in the instant application. Claims 1-17 and 52-55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on March 4, 2009. Accordingly, claims 18, 23-26, 32-33, and 56-71 are currently under examination on the merits in the instant case.

Response to Arguments

Applicant's arguments with respect to claims 18-20 and 22-34 filed on April 5, 2010 have been considered but are moot in view of claim amendments and the new ground(s) of rejection.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on May 25, 2010 is considered by the examiner.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 18, 23-26, 32-33, 56-67, and 69-71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Motzer et al. (*Journal of Clinical Oncology,* 2002, 20:289-296, applicant's citation) in view of Pyrhönen et al. (*Journal of Clinical Oncology,* 1999, 17:2859-2867, applicant's citation), Lorus Therapeutics Inc.'s press release (October 30, 2001, applicant's citation), Lorus Therapeutics Inc.'s press release (January 26, 2000, applicant's citation), and Wright et al. (US 5,998,383, citation of record).

Motzer et al. teach the following with regard to combination therapeutic approaches for renal cell carcinoma (RCC) at page 294: "Inteferon-α and interleukin-2 show a low degree of antitumor effect against RCC. Outcome data from either cytokine may be considered in clinical trial design and interpretation of new therapies." They further teach that one can design new combination therapeutic programs against metastatic RCC by combining new anti-cancer agents with interferon-α. They teach that it is an art-recognized goal to devise a new, more effective therapeutic approach for advanced RCC because of "the low proportion of patients with advanced RCC achieving long-term survival". See page 295. They teach that several RCC treatment strategies comprising subcutaneous or intramuscular IFN-α administration have been under clinical trials and they also disclose a phase II trial for combination of IFN-α and IL-2 as a first-line therapy. See Table 1. Motzer et al. do not teach metastatic or advanced RCC treatment method comprising administering an anti-R2 antisense compound in combination with IL-2, IFNalpha-2a, and a chemotherapeutic agent.

Pyrhönen et al. teach that the combination of IFNα-2a and vinblastine results in superior treatment effects (e.g., overall survival rate, progression-free survival rate) in patients with advanced or metastatic RCC compared to vinblastine alone. Similar to Motzer et al., Pyrhönen et al. teach that "the current treatment options for patients with advanced RCC are unsatisfactory." and therefore there is a great, essential need for further development of new treatment strategies for advanced RCC. See page 2866. They teach that vinblastine is administered intravenously and IFNα-2a is administered either subcutaneously or intramuscularly. See page 2860.

The Lorus Therapeutic Inc.'s press release of October 30, 2001 reports that GTI 2040 (identical in sequence to SEQ ID NO:1 claimed in the instant case) is effective for treating patients with advanced or metastatic renal cell carcinoma in a monotherapy and that GTI 2040 is highly likely to be tolerable when used in combination with a chemotherapeutic drug used to treat renal cell carcinoma. The press release also teaches that the FDA approved IL-2 drug, Proleukin, for renal cell carcinoma treatment has "severe side effects".

The Lorus Therapeutic Inc.'s press release of January 26, 2000 reports that GTI 2040 is "extremely effective against a wide range of different tumor types and showed complete tumor regressions when used in combination with certain chemotherapeutic agents."

Wright et al. teach a combination cancer therapeutic method comprising administering an anti-R2 antisense oligonucleotide of SEQ ID NO:42 (identical in sequence to SEQ ID NO:1 claimed in the instant case) and a chemotherapeutic drug (hydroxyurea, MTX, PALA) to a cancer patient, wherein the combination of the two agents (an antisense oligonucleotide and a chemotherapeutic drug) are more effective for cancer treatment whereas antisense alone is insufficient to inhibit tumor growth. See claims 11-13, 18-19, 21-23. They teach that "the R2 antisense sequence can also act synergistically with well known chemotherapeutic agents." See column 17, lines 33-34. They teach that phosphorothioate incorporation into an antisense oligonucleotide enhances nuclease resistance and pharmacokinetics. They teach that anti-R2 antisense oligonucleotides can be used to treat carcinomas of solid tissue and genitourinary cancers such as cervical and bladder cancer and that the antisense oligonucleotides can be administered parenterally including intravenous administration.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to additionally administer GTI 2040 to patients having advanced metastatic renal cell carcinoma in the combination therapy of Motzer et al. and Pyrhönen et al.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success so as to provide a better, prolonged survival rate for patients with advanced metastatic renal cell carcinoma (RCC), because IL-2 and/or IFN-alpha-based conventional treatment strategies for advanced metastatic RCC were found to be "unsatisfactory" as only "a low degree of antitumor effect against RCC" was shown and only "the low proportion of patients with advanced RCC achieving long-term survival" with "severe side effects" as taught by Motzer et al., Pyrhönen et al., and the Lorus Therapetuics Inc.'s press release (October 30, 2001), thereby suggesting that it was an art-recognized goal to devise new, more effective RCC treatment strategies, and because combination therapy comprising GTI2040 was suggested to be useful and effective for treating various solid tumors including advanced metastatic RCC as taught by the Lorus Therapetuics Inc.'s press releases and Wright et al. Further, the increased efficacy of a combination therapeutic approach for cancer treatment compared to a monotherapy was amply suggested in the art as taught by the combination comprising IFNα-2a and vinblastine of Pyrhönen et al., which is "superior" to vinblastine alone, or the combination comprising GTI2040 and chemotherapeutic agents, which "showed complete tumor regressions when used in combination with certain chemotherapeutic agents." as reported by the Lorus Therapetuics Inc.'s press release (January 26, 2000), wherein the combination of GTI2040 and a chemotherapeutic drug was shown to result in synergistic anti-cancer effects as taught by Wright

et al. In view of the foregoing, the claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Claims 18, 23-24, 26, 32-33, 56-63, 65-68, and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wright et al. (US 5,998,383, citation of record) in view of Dorigo et al. (*Gynecologic Oncology,* 1998, 71:204-210) and Salom et al. (*Current Opinion in Oncology,* 2002, 14:519-527).

Wright et al. teach a combination cancer therapeutic method comprising administering an anti-R2 antisense oligonucleotide of SEQ ID NO:42 (identical in sequence to SEQ ID NO:1 claimed in the instant case) and a chemotherapeutic drug (hydroxyurea, MTX, PALA) to a cancer patient, wherein the combination of the two agents (an antisense oligonucleotide and a chemotherapeutic drug) are more effective for cancer treatment whereas antisense alone is insufficient to inhibit tumor growth. See claims 11-13, 18-19, 21-23. They teach that "the R2 antisense sequence can also act synergistically with well known chemotherapeutic agents." See column 17, lines 33-34. They teach that phosphorothioate incorporation into an antisense oligonucleotide enhances nuclease resistance and pharmacokinetics. They teach that anti-R2 antisense oligonucleotides can be used to treat carcinomas of solid tissue and genitourinary cancers such as cervical and bladder cancer and that the antisense oligonucleotides can be administered parenterally including intravenous administration. Wright et al. do not teach further administering IL-2 for genitourinary tract cancer treatment.

Dorigo et al. teach a combination cancer treatment regimen comprising administering an antisense compound (anti-TGF-β) and IL-2 in the intraperitoneal model of murine ovarian

teratoma (MOT). They show that the combination of the two anti-cancer agents produces synergistic anti-cancer effects compared to either agent alone as the IL-2 alone resulted in a 33% tumor-free animals; the antisense alone resulted in zero % tumor-free animals; and the combination of IL-2 and antisense agents resulted in a 69% tumor-free animals. See Table 1 and Figure 3.

Salom et al. teach that intraperitoneal IL-2 has been tested in human patients with advanced stage ovarian cancer and that low doses of IL-2 in combination with monoclonal antibodies with adjuvant chemotherapy in advanced ovarian cancer patients have been clinically tested. See Table 9. They teach that IL-2 potentiates immune response and is well tolerated. See page 526.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to additionally administer IL-2 for the genitourinary tract cancer treatment method of Wright et al.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success so as to potentiate immune response in a patient with genitourinary tract cancer, thereby producing synergistic or additive anti-cancer effects when combined with the anti-R2 antisense oligonucleotide of SEQ ID NO:42 of Wright et al. and a chemotherapeutic drug, because the synergistic anti-cancer effects of the combination comprising SEQ ID NO:42 and a chemotherapeutic drug was explicitly suggested by Wright et al., and IL-2-based combination therapeutic strategies (for example, further comprising an antisense agent as taught by Dorigo et al., or further comprising a monoclonal antibody and chemotherapy as taught by Salom et al.) were shown to be significantly more effective than a single agent alone (e.g., IL-2

alone or antisense agent alone), and because IL-2 was taught to be helpful in combination therapeutic strategies for genitourinary tract cancer treatment as it potentiates immune response and is well tolerated as taught by Salom et al. Hence, one of ordinary skill in the art would have seen the benefits and advantages associated with synergistic treatment effects for administering IL-2 in combination with SEQ ID NO:42 of Wright et al. and a chemotherapeutic agent. Accordingly, the claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 18, 23-26, 32-33, and 56-71 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11-13 and 18-26 of U.S. Patent No. 5,998,383 in view of Motzer et al. (*Journal of Clinical Oncology,* 2002, 20:289-296, applicant's citation).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claims and the reference claims are drawn to a combination cancer therapeutic methods comprising administering SEQ ID NO:1 (identical to SEQ ID NO:42 in the reference claims). The differences between the instant claims and the reference claims are such that the reference claims do not specify that the "neoplastic cells in a patient" are of advanced metastatic renal carcinoma cells and do not specify that the "chemotherapeutic drug" includes IFN-alpha or IL-2. However, at the time of filing, it was known in the art to administer IFN-alpha and IL-2 to patients having advanced metastatic renal carcinoma and that it was also suggested in the art that a new combination therapeutic approach was in need. See Motzer et al. Further, the specification of 5,998,383 teaches that "neoplastic cells" include genitourinary

cancers. See column 9. As such, the instant claims would have been obvious in view of the reference claims and the teachings of Motzer et al.

Claims 18, 23-26, 32-33, and 56-71 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 31-73 of U.S. Patent No. 7,405,205 B2 in view of Motzer et al. (*Journal of Clinical Oncology,* 2002, 20:289-296, applicant's citation).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claims and the reference claims are drawn to a combination cancer therapeutic methods comprising administering SEQ ID NO:1 (identical to SEQ ID NO:42 in the reference claims). The differences between the instant claims and the reference claims are such that the reference claims do not specify that the "one or more chemotherapeutic drugs" include IFN-alpha or IL-2. However, at the time of filing, it was known in the art to administer IFN-alpha and IL-2 to patients having advanced metastatic renal carcinoma and that it was also suggested in the art that a new combination therapeutic approach was in need. See Motzer et al. As such, one of ordinary skill in the art would have been motivated to modify the reference claims to include IFN-alpha or IL-2 in combining with SEQ ID NO:42 for leukemia treatment or bladder cancer treatment or cervical cancer treatment or various solid cancer treatments including the RCC of Motzer et al. As such, the instant claims would have been obvious in view of the reference claims and the teachings of Motzer et al.

Claims 18, 23-26, 32-33, and 56-71 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 57-75 of copending Application No. 12/691,664. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claims and the reference claims are drawn to a combination cancer therapeutic methods comprising administering SEQ ID NO:1. Although the reference claims do not specifically recite administering IL-2 or IFN-alpha, the claims recite "comprising administering", wherein the transitional term "comprising" is open-ended and thus does not exclude any unrecited elements. In fact, the specification of 12/691,664 makes it clear that the claims embody administering IL-2 or IFN-alpha to the human patient. See Table 1. Hence, the scope of the instant claims and that of the reference claims overlap with each other. Further, although the claims are drawn to acute myeloid leukemia treatment methods, it would have been obvious to use the method steps of the reference claims to treat renal cell carcinoma or ovarian cancer as claimed in the instant case in view of the disclosure of 12/691,664. See Table 1. Hence, the instant claims are obvious variants of the reference claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, 7am-3:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low (Acting SPE) can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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